REMARKS

Examiner Interview Summary

The Examiner is thanked for the telephone interview on June 21, 2005, between the Examiner and Applicant's Representative, Victoria A. Sandberg. All pending claims were discussed.

Applicant's Representative reviewed the art of record as it pertains to the claimed method involving anaerobic production of polyhydroxyalkanoates in yeast. The meanings of the terms "fermentation" and "anaerobic" were discussed, as was the propriety of the use of bacterial art to support the art rejections when analogous claims directed to bacteria, instead of yeast, were restricted into a different group (Group VI) by the Examiner. Removal of the references as nonanalogous art, or alternatively rejoinder of the claims of Group VI, were discussed.

No agreement was reached; however, the Examiner agreed to consider an after-final response submitted by the Applicant.

Rejection under 35 U.S.C. §103(a)

The Examiner rejected claims 1-13 under 35 U.S.C. §103(a) as being unpatentable over Madison et al. (*Micro. Mol. Biol. Rev.*, 1999;*63*(1):21-53), Clemente et al. (U.S. Patent No. 5,849,892), and Lee et al. (*Int. J. Biol. Macromol.*, 1999;*25*(1-3):31-6). This rejection is respectfully traversed, for reasons already of record as well as those stated below.

Claim 1 is directed to the production of polyhydroxyalkanoates in a transgenic yeast cell under anaerobic culture conditions.

Madison et al. is a review article generally describing metabolic engineering of poly(3-hydroxyalkanoates) (PHAs). At page 44, citing Leaf et al. (Microbiology, 1996, 142:1169-1180), Madison et al. describe accumulation of P(3HB) by *Saccharomyces cerevisiae* cells when the P(3HB) polymerase gene from *R. eutropha* was introduced into the cells. Madison et al. note the low level of accumulation of P(3HB) in Leaf et al., and suggest that elevation of thiolase and reductase activities may lead to improved P(3HB) production in yeast.

Madison et al. do not teach anacrobic culture conditions. Indeed, Madison et al. is itself silent as to the culture conditions (aerobic vs. anaerobic) for production of PHB in yeast. However, the *S. cerevisiae* experiments that are reported in Madison et al. were conducted under *aerobic* conditions (Leaf et al. at page 1170: "Dissolved oxygen did not drop below 90% over the course of batch growth."). Neither Madison et al. nor the cited reference Leaf et al. suggest the use of anaerobic growth conditions to improve the observed low yield of polyalkanoates in yeast.

Both secondary references cited by the Examiner (i.e., Lee et al. and Clemente et al.) teach only bacterial systems. Yeast is not mentioned. Applicant submits that Lee et al. and Clemente et al., in that they teach bacterial systems when the elected invention recites polyhydroxyalkanoates in yeast, constitute nonanalogous art. Yeast and bacteria are substantially different organisms, one being prokaryotic while the other is eukaryotic; they require substantially different handling; and they have significantly different metabolisms. Anaerobic catabolism of pyruvate in bacteria for example has, as its end product, lactic acid, whereas the anaerobic catabolism of pyruvate in yeast produces ethanol. The present invention constitutes metabolic engineering and works a substantial change in the fatty acid metabolism of the host organism in order to produce the PHA. Anaerobic production of PHA is particularly complex, making techniques useful in one cell type difficult to apply to another cell type. As *E. coli* and *S. cerevisiae* are substantially different, both in terms of their culturing and their metabolism, and as anaerobic culturing provides further and often unpredictable complications, the cited references provide no reasonable expectation of success that PHA could be produced anaerobically in yeast. Additionally, because of the profound differences between bacterial systems and yeast, there is no reasonable expectation of success in achieving the claimed invention based on the combination of the cited references.

Furthermore, it is respectfully submitted that the Examiner has essentially already appreciated the substantial differences between production of PHA in bacteria and the production of PHA in yeast by restricting methods in yeast from methods in bacterial cells. Specifically, the claims of the present application were earlier subject to a restriction

requirement, in which claims 1-13 and 27-33 (Group I, to a method of producing PHA in transgenic *yeast*) were restricted from claims 62-67 and 78-83 (Group VI, to a method of producing PHA in transgenic *bacterial* cells) (emphasis added). The Examiner, on p. 4 of the restriction requirement, stated that "[t]he methods of inventions I-VIII are patentably distinct as directed to materially different methods employing different products. Inventions I-VIII are also patentably distinct from each other because the methods have different effects and utilities." As stated in M.P.E.P. § 802.01, "[t]he term "distinct" means that two or more subjects as disclosed are related ... but are capable of separate manufacture, use, or sale as claimed, AND ARE PATENTABLE (novel and unobvious) OVER EACH OTHER (though they may each be unpatentable because of the prior art)" (emphasis in the original). Thus, the Examiner's statement in the Office Action at p. 4-5, that "[a]lthough Lee et al. uses bacteria, one of ordinary skill in the art can apply similar methodology in producing polyhydroxyalkanoates using yeast in anaerobic conditions" is contradicted by the restriction earlier applied to the present application, in which anaerobic production of PHA was restricted between yeast and bacteria.

For at least the reasons provided above, reconsideration and withdrawal of the rejection of claims 1-13 under 35 U.S.C. §103(a) as being unpatentable over Madison et al. in view of Clemente et al. and Lee et al. is respectfully requested.

Summary

It is respectfully submitted that the pending claims 1-13 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives at the telephone number below, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that this paper is being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to: Commissioner for Patents, Mail Stop AF, P.O. Box 1450, Alexandria, VA 22313-1450, on this 24th day of June, 2005, at 11:40 a.m. (Central Time).

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